Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application. (While the nomenclature for the various RD NMR experiments recited in the claims contains portions that are underlined, they are not to be considered amendments to the claims.)

1.-90. (canceled)

91. (currently amended) A method for obtaining rapid and complete assignments of chemical shift values of ^{1}H, ^{13}C and ^{15}N of a protein molecule comprising:

providing a $^{15}N/^{13}C$-labeled protein sample; and

conducting four reduced dimensionality (RD) nuclear magnetic resonance (NMR) experiments on the protein sample, wherein (1) a first experiment is selected from the group consisting of a RD three-dimensional (3D) $H^{\alpha/\beta}C^{\alpha/\beta}$(CO)NHN NMR experiment, a RD 3D HA,CA,(CO),N,HN NMR experiment, and a RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment for obtaining sequential correlations of chemical shift values; (2) a second experiment is selected from the group consisting of a RD 3D HNNCAHA NMR experiment, a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,N,HN NMR experiment, and a RD 3D HNN<CO,CA> NMR experiment for obtaining intraresidue correlations of chemical shift values; (3) a third experiment is a RD 3D H,C,C,H-COSY NMR experiment for obtaining assignments of sidechain chemical shift values; and (4) a fourth experiment is a RD two-dimensional (2D) HB,CB,(CG,CD),HD NMR experiment for obtaining assignments of aromatic sidechain chemical shift values.

92. (original) The method according to claim 91 further comprising:

subjecting the protein sample to a RD 2D H,C,H-COSY NMR experiment for obtaining assignments of sidechain chemical shift values.

93. (original) The method according to claim 91, wherein the first experiment is the RD 3D $H^{\alpha/\beta}C^{\alpha/\beta}$(CO)NHN NMR experiment and the second experiment is the RD 3D HNNCAHA NMR experiment.

94. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D HA,CA,(CO),N,HN NMR experiment to distinguish between NMR signals for $^{1}H^{\alpha}/^{13}C^{\alpha}$ and $^{1}H^{\beta}/^{13}C^{\beta}$ from said RD 3D $H^{\alpha/\beta}C^{\alpha/\beta}$(CO)NHN NMR experiment.

95. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment to obtain assignments of chemical shift values of $^{1}H^{ali}$ and $^{13}C^{ali}$.

96. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,N,HN NMR experiment to obtain assignments of chemical shift values of $^{1}H^{\beta}$ and $^{13}C^{\beta}$.

97. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

98. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

99. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment and a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of $^{13}C'$.

100. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aliphatic sidechains.

101. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aromatic sidechains.

102. (original) The method according to claim 93 further comprising:

subjecting the protein sample to a 3D HNNCACB NMR experiment to obtain assignments of chemical shift values of $^{13}C^{\beta}$.

103. (original) The method according to claim 93, wherein the first experiment is the RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment and the second experiment is the RD 3D HNNCAHA NMR experiment.

104. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D HA,CA,(CO),N,HN NMR experiment to identify NMR signals for $^{1}H^{\alpha}/^{13}C^{\alpha}$ in said RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment.

105. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,N,HN NMR experiment to obtain assignments of chemical shift values of $^{1}H^{\beta}$ and $^{13}C^{\beta}$.

106. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

107. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

108. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment and a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of $^{13}C'$.

109. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aliphatic sidechains.

110. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aromatic sidechains.

111. (original) The method according to claim 103 further comprising:

subjecting the protein sample to a 3D HNNCACB NMR experiment to obtain assignments of chemical shift values of $^{13}C^{\beta}$.

112. (original) The method according to claim 91, wherein the first experiment is the RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment and the second experiment is the RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,N,HN NMR experiment.

113. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D HA,CA,(CO),N,HN NMR experiment to identify NMR signals for $^{1}H^{\alpha}$ and $^{13}C^{\alpha}$ in said RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment.

114. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}C^{\alpha/\beta}$(CO)NHN NMR experiment to identify NMR signals for $^{1}H^{\alpha/\beta}$ and $^{13}C^{\alpha/\beta}$ in said RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment.

115. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

116. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

117. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D HNN<CO,CA> NMR experiment and a RD 3D $H^{\alpha/\beta}$,$C^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of $^{13}C'$.

118. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aliphatic sidechains.

119. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aromatic sidechains.

120. (original) The method according to claim 112 further comprising:

subjecting the protein sample to a 3D HNNCACB NMR experiment to obtain assignments of chemical shift values of $^{13}C^{\beta}$.

121. (original) The method according to claim 91, wherein the first experiment is the RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment and the second experiment is the RD 3D HNN<CO,CA> NMR experiment.

122. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a RD 3D HA,CA,(CO),N,HN NMR experiment to identify NMR signals for $^{1}H^{\alpha}$ and $^{13}C^{\alpha}$ in said RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment.

123. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a RD 3D $H^{\alpha/\beta}C^{\alpha/\beta}$(CO)NHN NMR experiment to identify NMR signals for $^{1}H^{\alpha/\beta}$ and $^{13}C^{\alpha/\beta}$ in said RD 3D H,C,(C-TOCSY-CO),N,HN NMR experiment.

124. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a RD 3D $\underline{H}^{\alpha/\beta}$,$\underline{C}^{\alpha/\beta}$,CO,HA NMR experiment to obtain assignments of chemical shift values of polypeptide backbone carbonyl carbons, $^{13}C'$.

125. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aliphatic sidechains.

126. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a RD 3D H,C,C,H-TOCSY NMR experiment to obtain assignments of chemical shift values of ^{1}H and ^{13}C of aromatic sidechains.

127. (original) The method according to claim 121 further comprising:

subjecting the protein sample to a 3D HNNCACB NMR experiment to obtain assignments of chemical shift values of $^{13}C^{\beta}$.

128. (original) The method according to claim 91 further comprising:

subjecting the protein sample to nuclear Overhauser effect spectroscopy (NOESY) to deduce the tertiary structure of the protein molecule.

129. (original) The method according to claim 91 further comprising:

subjecting the protein sample to NMR experiments that measure scalar coupling constants to deduce the tertiary structure of the protein molecule.

130. (original) The method according to claim 91 further comprising:

subjecting the protein sample to NMR experiments that measure residual dipolar coupling constants to deduce the tertiary structure of the protein molecule.

131. (previously presented) The method according to claim 91, wherein said 3D H,C,C,H-COSY NMR experiment is conducted by a method of measuring the chemical shift values for $^{1}H^{m}$, $^{13}C^{m}$, $^{1}H^{n}$, and $^{13}C^{n}$ of a protein molecule wherein *m* and *n* indicate atom numbers of two CH, CH_2 or CH_3 groups that are linked by a single covalent carbon-carbon bond in an amino acid residue, said method comprising:

providing a protein sample;

applying radiofrequency pulses to the protein sample which effect a nuclear spin polarization transfer wherein the chemical shift evolutions of $^{1}H^{m}$ and $^{13}C^{m}$ are connected to the chemical shift evolutions of $^{1}H^{n}$ and $^{13}C^{n}$, under conditions effective (1) to generate NMR signals encoding the chemical shift values of $^{13}C^{m}$ and $^{13}C^{n}$ in a phase sensitive manner in two indirect time domain dimensions, $t_1(^{13}C^{m})$ and $t_2(^{13}C^{n})$, respectively, and the chemical shift value of $^{1}H^{n}$ in a direct time domain dimension, $t_3(^{1}H^{n})$, and (2) to cosine modulate the chemical shift evolution of $^{13}C^{m}$ in $t_1(^{13}C^{m})$ with the chemical shift evolution of $^{1}H_{m}$; and

processing the NMR signals to generate a 3D NMR spectrum with peak pairs derived from said cosine modulating wherein (1) the chemical shift values of $^{13}C^{n}$ and $^{1}H^{n}$ are measured in two frequency domain dimensions, $\omega_2(^{13}C^{n})$ and $\omega_3(^{1}H^{n})$, respectively, and (2) the chemical shift values of $^{1}H^{m}$ and $^{13}C^{m}$ are measured in a frequency domain dimension, $\omega_1(^{13}C^{m})$, by the frequency differences between the two peaks forming said peak pairs and the frequencies at the center of the two peaks, respectively.

132. (previously presented) The method according to claim 91, wherein said 2D HB,CB,(CG,CD),HD NMR experiment is conducted by a method of measuring the chemical shift values for the following nuclei of a protein molecule : (1) a β-proton of an amino acid residue with an aromatic side chain, $^{1}H^{\beta}$; (2) a β-carbon of an amino acid residue with an aromatic side chain, $^{13}C^{\beta}$; and (3) a δ-proton of an amino acid residue with an aromatic side chain, $^{1}H^{\delta}$, said method comprising:

providing a protein sample;

applying radiofrequency pulses to the protein sample which effect a nuclear spin polarization transfer wherein the chemical shift evolutions of $^{1}H^{\beta}$ and $^{13}C^{\beta}$ are connected to the chemical shift evolution of $^{1}H^{\delta}$, under conditions effective (1) to generate NMR signals encoding the chemical shift value of $^{13}C^{\beta}$ in a phase sensitive manner in an indirect time domain dimension, $t_1(^{13}C^{\beta})$, and the chemical shift value of $^{1}H^{\delta}$ in a direct time domain dimension, $t_2(^{1}H^{\delta})$, and (2) to cosine modulate the chemical shift evolution of $^{13}C^{\beta}$ in $t_1(^{13}C^{\beta})$ with the chemical shift evolution of $^{1}H^{\beta}$; and

processing the NMR signals to generate a 2D NMR spectrum with a peak pair derived from said cosine modulating wherein (1) the chemical shift value of $^{1}H^{\delta}$ is measured

in a frequency domain dimension, $\omega_2(^1H^{\delta})$, and (2) the chemical shift values of $^1H^{\beta}$ and $^{13}C^{\beta}$ are measured in a frequency domain dimension, $\omega_1(^{13}C^{\beta})$, by the frequency difference between the two peaks forming said peak pair and the frequency at the center of the two peaks, respectively.